BioMarin Announces Oral Presentation of 2-Year Analysis of Largest Phase 3 Gene Therapy Study in Adults with Severe Hemophilia A at 15th Annual Congress of European Association for Haemophilia and Allied Disorders (EAHAD) 2-4 February

- Improved Bleed Free Rate from 32% at Baseline Maintained Through Year 1 (82%) and Year 2 (84%)

- Factor VIII Treatment Burden Compared to Baseline Reduced by 98%

- 95% of Study Participants Remain Off Standard of Care Factor VIII Prophylactic Therapy

SAN RAFAEL, Calif., Feb. 4, 2022 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) today announced that the Company presented positive results from a two-year analysis of the Phase 3 GENEr8-1 study and an overall safety update of valoctocogene roxaparvovec, an investigational gene therapy for the treatment of adults with severe hemophilia A, at the 15th Annual Virtual Congress of the European Association for Haemophilia and Allied Disorders (EAHAD). This is the largest global Phase 3 study to date for any gene therapy in hemophilia with 134 participants.

In the GENEr8-1 Phase 3 study, Annualized Bleeding Rate (ABR) was significantly reduced by 4.1 treated bleeds per year (p-value <0.0001), or by 85% from a baseline mean of 4.8 (median 2.8), in the pre-specified primary analysis in participants from a prior non-interventional study (rollover population; N=112; median follow-up of 110 weeks). The percentage of participants with zero treated bleeds increased from 32% on prophylaxis at baseline to 82% during year 1 and 84% during year 2. The mean ABR was 0.8 (median 0.0) through the entire efficacy evaluation period, 0.9 (median 0.0) during year one, and 0.7 (median 0.0) during year two.

Across all participants in the rollover population (N=112), mean annualized Factor VIII infusion rate was reduced by 133 infusions per year (p-value <0.0001) or 98% from baseline. As of the two-year data cut, 95% of participants remain off Factor VIII prophylactic therapy.

"This data demonstrates sustained bleed control is possible at the lower limits of quantification of Factor VIII activity, which may be the start of understanding the durability of gene therapy in hemophilia A, particularly with valoctocogene roxaparvovec," said Prof. Johnny Mahlangu, a study investigator and Professor in

Haematology and Head of School of Pathology in the Faculty of Health Sciences of the University of the Witwatersrand in Johannesburg, South Africa. "I am pleased to see that a high level of study participants remains off prophylaxis reducing the burden of injecting themselves over a hundred times a year."

"We are pleased to share these transformational data at EAHAD that show this important advance for more than 80% of study participants, who are bleed free and more than 95%, who do not require Factor VIII prophylactic therapy," said Hank Fuchs, M.D., President of Worldwide Research and Development at BioMarin. "Such outcomes are not afforded by any currently available therapy."

Valoctocogene Roxaparvovec Safety

All participants in the Phase 3 study received a single 6e13 vg/kg dose. No participants developed inhibitors to Factor VIII, malignancy, or thromboembolic events. During year two, no new safety signals emerged, and no treatment-related serious adverse events (SAE) were reported. Most patients had discontinued any corticosteroid (CS) use in year one, and there were no CS-related SAEs in the remaining patients being tapered off CS in year two. Overall, the most common adverse events (AE) associated with valoctocogene roxaparvovec occurred early and included transient infusion associated reactions and mild to moderate rise in liver enzymes with no long-lasting clinical sequelae. Alanine aminotransferase (ALT) elevation (119 participants, 89%), a laboratory test of liver function, remained the most common AE. Other common adverse events were headache (55 participants, 41%), arthralgia (53 participants, 40%), nausea (51 participants, 38%), aspartate aminotransferase (AST) elevation (47 participants, 35%), and fatigue (40 participants, 30%). In a Phase 1/2 study, an SAE of a salivary gland mass was identified in one study participant, who was treated more than five years ago, and was reported as unrelated to valoctocogene roxaparvovec by the investigator. The relevant health authorities were notified in late 2021, and all studies remain ongoing without modification. The independent Data Monitoring Committee (DMC) further reviewed the case. A genomic analysis is being conducted as prespecified in the clinical trial protocol.

GENEr8-1 Study Description

The global Phase 3 GENEr8-1 study evaluates superiority of valoctocogene roxaparvovec at the 6e13 vg/kg dose compared to the current standard of care, FVIII prophylactic therapy. All study participants had severe hemophilia A at baseline, defined as less than or equal to 1 IU/dL of Factor VIII activity. The study included 134 total participants, all of whom had a minimum of 24 months of follow-up at the time of the data cut. The first 22

participants were directly enrolled into the Phase 3 study, 17 of whom were HIV-negative and dosed at least 36 months or 3 years prior to the data cut date. The remaining 112 participants (rollover population) completed at least six months in a separate non-interventional study to prospectively assess bleeding episodes, Factor VIII use, and health-related quality of life while receiving Factor VIII prophylaxis prior to rolling over to receive a single infusion of valoctocogene roxaparvovec in the GENEr8-1 study.

About Hemophilia A

People living with hemophilia A lack sufficient functioning Factor VIII protein to help their blood clot and are at risk for painful and/or potentially life-threatening bleeds from even modest injuries. Additionally, people with the most severe form of hemophilia A (FVIII levels <1%) often experience painful, spontaneous bleeds into their muscles or joints. Individuals with the most severe form of hemophilia A make up approximately 50 percent of the hemophilia A population. People with hemophilia A with moderate (FVIII 1-5%) or mild (FVIII 5-40%) disease show a much-reduced propensity to bleed. The standard of care for individuals with severe hemophilia A is a prophylactic regimen of replacement Factor VIII infusions administered intravenously up to two to three times per week or 100 to 150 infusions per year. Despite these regimens, many people continue to experience breakthrough bleeds, resulting in progressive and debilitating joint damage, which can have a major impact on their quality of life.

Hemophilia A, also called Factor VIII deficiency or classic hemophilia, is an X-linked genetic disorder caused by missing or defective Factor VIII, a clotting protein. Although it is passed down from parents to children, about 1/3 of cases are caused by a spontaneous mutation, a new mutation that was not inherited. Approximately 1 in 10,000 people have Hemophilia A.

About BioMarin

BioMarin is a global biotechnology company that develops and commercializes innovative therapies for serious and life-threatening rare and ultra-rare genetic diseases. The Company's portfolio consists of seven commercialized products and multiple clinical and pre-clinical product candidates. For additional information, please visit www.biomarin.com. Information on BioMarin's website is not incorporated by reference into this press release.

Forward Looking Statements

This press release contains forward-looking statements about the business prospects of BioMarin Pharmaceutical Inc., including without limitation, statements about the development of BioMarin's valoctocogene roxaparvovec program generally, the data presented at EAHAD, the impact of valoctocogene roxaparvovec gene therapy for treating patients with severe hemophilia A, the potential for valoctocogene roxaparvovec to reduce or eliminate bleeds at the lower limits of quantification of Factor VIII activity, reduce the number of Factor VIII infusions, the predictive value of the Phase 1/2 study, understanding the durability of gene therapy in hemophilia A, particularly with valoctocogene roxaparvovec, and the ongoing clinical programs generally. These forward-looking statements are predictions and involve risks and uncertainties such that actual results may differ materially from these statements. These risks and uncertainties include, among others: results and timing of current and planned preclinical studies and clinical trials of valoctocogene roxaparvovec, including final analysis of the above data and additional data from the continuation of these trials and the entire development program, including further assessment of safety events, any potential adverse events observed in the continuing monitoring of the patients in the clinical trials; the content and timing of decisions by the FDA, the EMA and other regulatory authorities; the content and timing of decisions by local and central ethics committees regarding the clinical trials; our ability to successfully manufacture valoctocogene roxaparvovec; and those other risks detailed from time to time under the caption "Risk Factors" and elsewhere in BioMarin's Securities and Exchange Commission (SEC) filings, including BioMarin's Annual and quarterly Reports on Forms 10-K and 10-Q, and future filings and reports by BioMarin. BioMarin undertakes no duty or obligation to update any forward-looking statements contained in this press release as a result of new information, future events or changes in its expectations.

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